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HEAVY METAL TOXICITY AND THEIR HARMFUL EFFECTS ON LIVING ORGANISMS – A REVIEW

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ABSTRACT:

The contamination chain of heavy metals almost always follows cyclic order in the environment as industry, atmosphere, soil, water, foods and human. As it is clear that chronic exposure to heavy metals and metalloids at low levels cause the adverse effects. Heavy metals have been proved to be toxic to human and environmental health. Heavy metal toxicity is regarded as major threat and there is several health risks associated with it. Sometimes they may act as pseudo elements of the body but event at certain times they may interfere with metabolic processes. Few metals, like aluminum, can be removed by elimination activities, while some of the metals get accumulated in the body and food chain, exhibiting a chronic nature. Different public health procedures have been taken to control, prevent and treat metal toxicity which occurs at various levels, such as occupational exposure and environmental factors. Metal toxicity depends on the dose absorbed, route of exposure and duration of the exposure, which can lead to different disorders and results in excessive damage due to oxidative stress induced by free radical formation. This review provides insight into the sources of heavy metals and their harmful effects on environment and living organisms.

Key words: heavy metals, metal toxicity, oxidative stress, free radicals

1: Introduction

Metals constituting important class of the toxic substances encountered day to day life during occupational and environmental circumstances. The impact of such toxic agents on human health is presently an area of passionate interest because of ubiquity of its exposure, by increasing the use of wide verity of the metals in industry and in daily life work hood (Guan *et al*. 2001, Yan *et al*. 2008 and Christoforidis *et al* 2009). Heavy metals are significant environmental pollutants and toxicity of theirs is major problem for ecological, evolutionary, nutritional and environmental balances (Goyer 2001 and Wang *et al*. 2001). In waste water commonly found heavy metals include, cadmium, arsenic, chromium, lead, copper, zinc and nickel, all of these are causing risks to human health and the environmental balance by entering the surroundings via natural means and through the human activities (Beyersmann *et al*. 2008). Various natural and human day today activity sources of heavy metals include erosion of soil, natural weathering of the earth's crust, industrial effluents, mining, urban runoff, sewage discharge, insect or disease controlling agents, which are applied to crops (Arruti *et al*. 2010). Irrespective of these metals have essential biological functions with their least concentration in plants and animals, also occasionally their chemical coordination and oxidation-reduction properties of them have given an additional benefit. These metals get attached with the protein sites instead of their specific metals by displacing the original metals from their natural binding sites which causes the malfunctioning of the cells and ultimately cause toxicity. Earlier and latest research reports have found that oxidative deterioration in biological macromolecules is primarily due to the binding of heavy metals to the cellular components as structural proteins, enzymes, and nucleic acids and later interfere with their functioning. Long term exposure with the heavy metals can have

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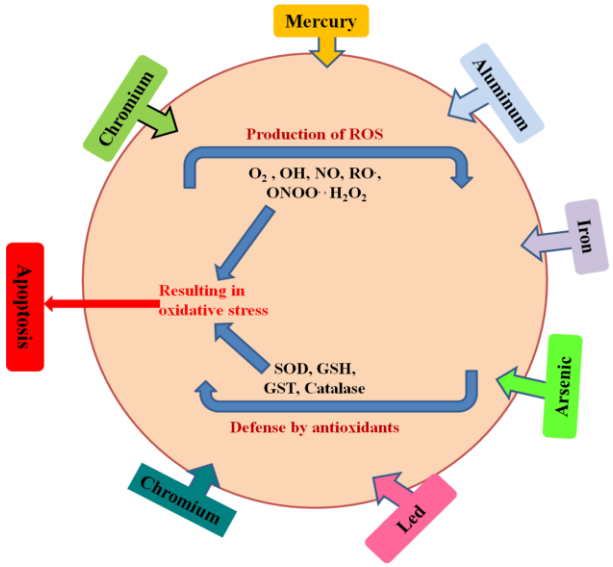
hazardous effects like carcinogenic, circulatory and central & peripheral nervous system.

2: Heavy metals, toxicity mechanisms and their Effects on humans

As numerous agricultural, domestic, medical, industrial, and technological applications have lead to extensive distribution of heavy metals within environment due to this there is raising major direct concerns over their potential effects on the human health and environment. Numerous factors including the chemical species, dose, route of exposure of heavy metals as well as the age, gender, genetics, and nutritional status of the exposed individuals depends up on the toxicity of heavy metals. In current scenario arsenic, cadmium, chromium, lead, and mercury are ranked as priority metals because of their high degree of toxicity which is becoming the major public health concern. These metallic elements are measured in systemic toxicants because they are known to induce multiple organ damage, even at very low exposure. When heavy metals are not metabolized by the body they become toxic and accumulate in soft tissues as they enter the human body in the course of food, water, air, or absorption through the skin.

There are thirty five metals that are of our concern because of the residential or occupational exposure, out of which most belongs to heavy metals (arsenic, bismuth, antimony, cerium, cadmium, chromium, cobalt, copper, gold, gallium, iron, manganese, lead, mercury, nickel, platinum, silver, tellurium, thallium, tin, uranium, vanadium, and zinc) and are commonly found in environment and diet (Showkat *et al*. 2017). In small amounts these metals are necessary for maintaining the good health but in the bigger amounts they can become toxic or dangerous to human health. Toxicity of heavy metals can lesser the energy levels and can damage the functioning of brain, kidney, lungs, liver, blood composition and other significant organs. Continuing exposure of some metals may lead to progressively progressing physical, muscular and neurological degenerative processes that replicate the diseases such as multiple sclerosis, Alzheimer's disease, Parkinson's disease and muscular dystrophy. Frequent long-term exposure of some metals and their compounds may even cause cancer (Ghosh *et al*. 2007).

Hence detailed knowledge/information of heavy metals is rather significant for allowing appropriate defensive measures against their excessive contact with human body (Ferrara 2000).



The attack of heavy metals on a cell and the balance between ROS production and the subsequent defense presented by antioxidants.

2.1: Arsenic

Arsenic is semi-metallic in nature and is among one of the most significant heavy metal, causing alarm from both the ecological and individual health as it is prominently toxic and carcinogenic, generally available in the form of oxides or sulfides or as a salt of iron, calcium, copper, sodium etc. Since it is the twentieth most abundant element on the earth and it is lethal in inorganic forms such as arsenite and arsenate compounds to both environment and living creatures (Kapaj *et al*. 2006 and Bhattacharya *et al*. 2007). Humans may come across with the arsenic by natural resources, industrial source, or from the unintended sources. Drinking water may get polluted by use of arsenical pesticides, common mineral deposits or unseemly transfer of arsenical chemicals (Casado-Martinez *et al*. 2010 and Mudhoo *et al*. 2011). By the deliberate utilization of arsenic in case of suicidal attempts or accidental consumption by children may too cause intense harming and its protoplasmic

poison nature it affects basically the sulphydryl gather of cells causing malfunctioning of cell respiration, cell enzymes and mitosis (Walker *et al*. 2010).

2.1.1: Mechanism of arsenic toxicity

Due to biotransformation of arsenic the risky inorganic arsenic compounds get methylated via algae, fungi, bacteria and humans to give the monomethylarsonic acid (MMA) and dimethylarsinic acid (DMA). During this biotransformation procedure inorganic arsenic species (iAs) are enzymetically changed to methylated arsenicals which are the end metabolites and are used as biomarker for chronic arsenic exposure.

Methylated end products of inorganic arsenic (MMA-III, MMA-V and DMA-V) during biomethylation detoxification process are excreted via urine and are bioindication of chronic arsenic exposure, but MMA (III) is not excreted and remains inside the body cells as an intermediate product. An intermediate product monomethylarsonic acid (MMA III) is of high toxicity as compared to other arsenicals and is potentially responsible for arsenic-induced carcinogenesis (Singh *et al*. 2007 and Uneyama *et al*. 2007).

iAs (V) → iAs (lll) MMA (V) → MMA (lll) → DMA (V)

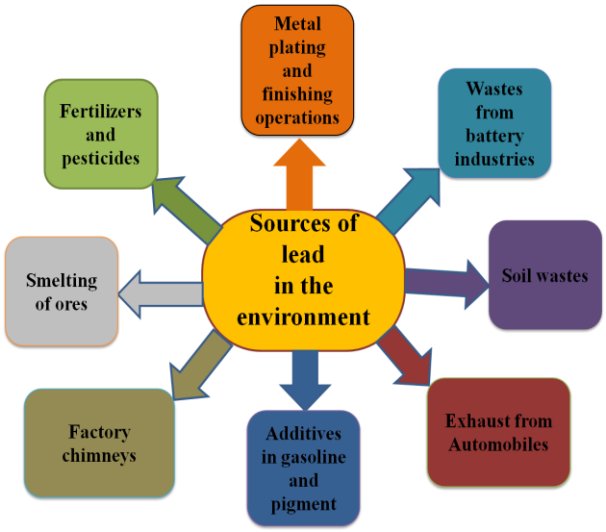
2.1.2: Effects of Arsenic on humans

The contaminations of arsenic occur on earth as a result of the natural geological processes and manmade activities. The anthropogenic sources of arsenic include activities of human (mining and processing of ores). The smelting an ancient and recent process can release the arsenic to air and soil (Matschull et at. 2000). These all types of sources can affect the quality of surface water by the use of groundwater ejection and runoff, other way of ground water contamination include geologic sources such as arsenic minerals and third type of the sources is sedimentary and meta-sedimentary bed rocks (Chowdhury *et al*. 200). Majority of the soaps, dyes, paints, metals, semi-conductors and drugs are containing arsenic and certain fertilizers, pesticides and animal feeding operations also release arsenic to the environment in higher amounts. But inorganic forms of arsenic such as the arsenite and arsenate are found to be extra hazardous to the human health as they are exceedingly carcinogenic to humans and may cause cancer of bladder, liver, lungs and skin (Stevens *et al*. 2010). Human beings are exposed to arsenic by means of air, food and water, among them contaminated drinking water with arsenic is one of the key causes for arsenic toxicity in more than thirty countries in the world (Henson *et al*. 2004 & Hoque *et al*. 2011). The improper disposal of arsenical chemicals, arsenical pesticides contaminated the water or it may be due to natural mineral deposits (Simone *et al*. 2010). Arsenic toxicity can be either acute or chronic; the chronic toxicity is termed as arsenicosis as most of the reports of arsenicosis in man focus on skin manifestations because of its specificity in diagnosis. The pigmentation and keratosis are the exact skin lesions that indicate the chronic arsenic toxicity in humans (Martin *et al*. 2009). Exposure of arsenic in low levels can cause nausea and vomiting, hands and legs pricking sensation, production of erythrocytes and leukocytes in lesser quantity, heart beat abnormality and blood vessels damage. While the long term exposure of arsenic can lead to neurological problems, formation of the skin lesions, peripheral vascular disease, pulmonary disease, hypertension and cardiovascular disease, diabetes mellitus and internal cancers (Sakurai *et al*. 2004 and Young *et al*. 2014) The chronic arsenicosis of arsenic many lead to permanent changes in the body vital organs due to which death rate is increases because of this lethal toxicity, there is no effective early treatment (Mohamed *et al*. 2011).

2.2: Lead

Lead (Pb) on routine basis used for storage batteries, ammunition, cable coverings, plumbing, nuclear reactors, paints and manufacture of tetraethyl Pb, radiation shields around X-ray equipment. An oxide of lead is used in producing fine crystal glass and flint glass, solder and insecticides. Lead is highly toxic metal and its routine use has caused excess environmental contamination and health related problems in many parts of the globe (Sharma *et al*. 2005)**.** The main source of lead exposure includes industrial

processes, food and smoking, drinking water and domestic sources and daily house based sources of lead were gasoline and house paint, which has been extended to lead bullets, pewter pitchers, plumbing pipes, toys, storage batteries and faucets **(**Jacobs *et al*. 2002).



Various sources of lead pollution in the environment

Vehicle exhausts released tons of lead per year in many parts of the world, in which some fraction is taken up by plants, fixation to soil and some fraction flow into water bodies, hence human exposure of lead in general population is either due to the food or drinking water (Goyer *et al*. 1990). Lead is an enormously toxic heavy metal and disturbs various plant physiological processes as latest research was revealed that lead is capable of inhibiting the growth of tea plant by reducing biomass and debases the tea quality by changing the quality of its components (Markowitz 2000, Najeeb *et al*. 2017 & Yongsheng *et al*. 2011). In plants there is enormous instability in the ion uptake by low concentration lead treatment and leads to significant metabolic changes in the photosynthetic capacity which intern causes strong inhibition of plant growth.

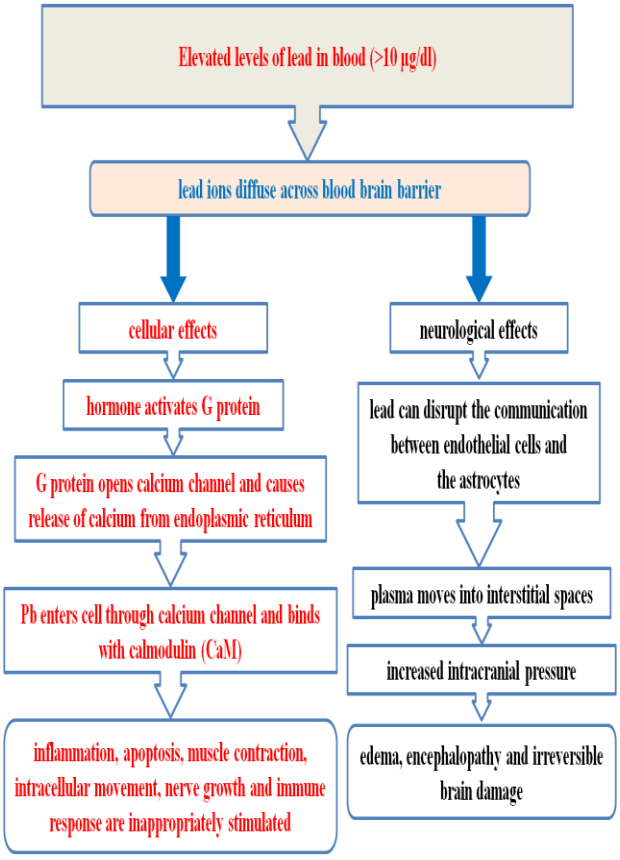
2.2.1: Mechanisms of lead toxicity

The lead toxicity is caused ionic and oxidative stress mechanisms in living cells. The oxidative stress in living cells occurs due to the imbalance in the production of free radicals and creation of antioxidants to detoxify the reactive intermediates. Presence of antioxidants like glutathione, in the living cells protects them from free radicals (e.g. H_2O_2). The reactive oxygen species (ROS) level increases and the level of antioxidants decrease due to the influence of lead.

The reduced form of glutathione (GSH) gives its reducing equivalents ($H^+ + e^-$) from thiol groups of cystein to reactive oxygen species and making them stable. In presence of the enzyme glutathione peroxidases glutathione is reduced, this reduced form is readily binds with other molecule of glutathione and form glutathione disulfide (GSSG).

The GSH reduced form of glutathione accounts for 90% of the total glutathione content as (GSSG) oxidized form accounts only 10% under normal conditions. However under oxidative stress conditions, GSSG concentration exceeds the GSH concentration Lipid peroxidation is another biomarker for oxidative stress, as free radical collects electron from the lipid molecules present inside cell membrane and eventually causes lipid peroxidation (Wadhwa *et al*. 2012). The high concentrations of reactive oxygen species may cause the structural damage to the cells and cellular components (proteins, nucleic acids, membranes and lipids) which results in a stressed situation at the cellular level (Mathew *et al* 2011)**.**

The ionic mechanism of the lead toxicity occurs principally with the ability of lead metal ions to replace other bivalent cations ($Ca2^+$, $Mg2^+$, Fe^{2+}) and monovalent cations (Na^+) which intern ultimately disturbs the biological metabolism of the living cells. This ionic lead toxicity also causes considerable changes in cell adhesion, intra- and inter-cellular signaling, protein folding, maturation, apoptosis, ionic transportation, enzyme regulation, and release of neurotransmitters. Ionic lead toxicity may also substitute calcium even in picomolar concentration which affects the protein kinase C which intern influence the neural excitation and memory storage (Flora *et al*. 2008).



Effects of increased lead level in blood

2.2.1: Effects of Lead on humans

Lead is highly toxic metal to living creature for this reason nowadays its use in various products (paints, gasoline etc) has been considerably reduced. But till date the main source of lead exposure are mining, fossil fuel burning, lead based paints, gasoline, cosmetics, ammunitions, solder, contaminated soil, industrial emission(Oehlenschlager *et al*. 2002, Raymond *et al*. 2011 and Gerhardsson *et al*. 2002). Now a day's lead poisoning is considered as a classic disease and signs which are seen within children and adults are essentially pertaining to the nervous system and gastrointestinal tract (Castro *et al*. 2008). The lead poisoning occurs also from the drinking water because the pipes which carry the water, if made up of lead and its compounds which can contaminate the water (Brochin *et al*. 2008). As per the Environmental Protection Agency (EPA) the lead is consider a potent carcinogenic factor and it affects major different parts of body because its distribution in body primarily depends on blood flow in the various tissues and nearly ninety five percent of lead is deposited in the skeletal bones in the form of insoluble phosphate (Arif *et al*. 2015). Lead Toxicity can be acute or chronic, the acute one can cause loss of hypertension, appetite, abdominal pain, headache, renal dysfunction, fatigue, arthritis, sleeplessness , hallucinations and vertigo, this acute exposure of lead mainly occurs in some place of work and in manufacturing industries were lead is used during manufacturing. The Chronic exposure of the lead can result in birth defects, mental retardation, psychosis, autism, hyperactivity, dyslexia, allergies, paralysis, weight loss, muscular weakness, kidney damage, brain damage may occur due to this chronic exposure of lead and even may cause death (Robert *et al*. 2008). Though lead poisoning is preventable but still it remains a dangerous threat of poisoning as it can affect most of the organs. The plasma membrane of the brain moves towards the interstitial spaces when blood brain barrier is exposed to the high levels of lead concentration and results in an edema, which disrupts the intracellular second messenger systems and alter the functioning of central nervous system, whose protection is highly important. The main sources of lead ions are environmental and domestic which becomes the main cause of disease but with proper precautionary measures it is possible to reduce the risk associated with the lead toxicity (Octavianti *et al*. 2010).

2.3: Mercury

The mercury (Hg) is a ubiquitous, very persistent element which can be found literally everywhere. It is a naturally occurring metal on earth, shiny silver-white, odorless liquid and becomes colorless and odorless gas on heating. It is highly toxic and exceedingly bioaccumulative in nature (Sutton *et al*. 2002). There is presence of adverse affects of mercury on marine environment and hence many latest research projects in the world studies are directed towards the distribution of mercury in water environment. The key source of the mercury pollution includes anthropogenic actions including agriculture, municipal wastewater discharges, mining, discharges of industrial wastewater and incineration. Mercury mainly exists as metallic elements, inorganic salts

and organic compounds; each of them possesses different toxicity and bioavailability (Lash *et al*. 2007). Presently all three forms of mercury are widely present in the water resources such as lakes, rivers and oceans, they were taken up by the microorganisms and get transformed into the methyl-mercury within the microorganisms, eventually undergoing biomagnifications causing significant disturbance to aquatic lives which creates imbalance in aquatic environment. The major route of human exposure to methyl mercury is the utilization of this contaminated aquatic animal by humans (Trasande *et al*. 2005). Routinely mercury is used in thermometers, barometers, hydrometers, pyrometers, fluorescent lamps, mercury arc lamps, and it is also being used in the pulp and paper industries as a component of batteries and in dental preparations such as amalgams.

2.3.1: Mechanism of mercury toxicity

Mercury is well known hazardous metal on earth because its toxicity is a frequent cause of acute heavy metal poisoning. It is one of the neurotoxic compounds responsible for, lipid peroxidation, mitochondrial damage, microtubule destruction and accumulation of neurotoxic molecules (serotonin, aspartate, and glutamate). The entire amount of the mercury production in the environment has been assessed at 2,200 metric tons yearly (Zahir *et al*. 2005). Animals that are exposed to toxic mercury environment have shown an adverse neurological and behavioral change, it is because brain remains the main target organ for the mercury, yet it can impair any organ and lead to malfunctioning of nerves, muscles and kidneys (Gagan *et al*. 2016). Mercury sometimes can also cause disruption within the membrane potential and interrupt with the intracellular homeostasis of calcium (Clarkson *et al*. 2003). The vapors of mercury can cause asthma, bronchitis and sometimes temporary respiratory problems. It plays a key role in damaging of tertiary and quaternary structure of the proteins and cellular functioning is altered by attachment of it to the selenohydryl and sulfhydryl groups, which undergo reaction with methyl mercury and hamper the cellular structure (Sarkar *et al*. 2005). It intervenes with the transcription and translation processes resulting in the disappearance of the ribosomes which causes the eradication of the endoplasmic reticulum and activity of natural killer cells (Holmes *et al*. 2009). As the beginning for heavy metal chelation, even though the mercury sulfhydryl bond is stable and divided into neighboring sulfhydryl consisting ligands, it also contributes free sulfhydryl groups to promote the metal mobility within ligands (Swaran *et al*. 2010).

2.3.2: Effects of Mercury on humans

Mercury is released in the environment via activities of various industries (pharmaceuticals, paper and pulp preservatives, agriculture industry, and chlorine and caustic soda production industry). It is considered one of the most toxic heavy metal in the environment (Morais *et al*. 2012). Mercury has the ability to combine with the other elements and form organic and inorganic mercury, exposure to this metallic, organic and inorganic mercury can damage kidneys, brain and developing fetus (Alina *et al*. 2012). Mercury is present almost in all foods and beverages within the range <1 to 50 µg/kg while in the marine foods mercury is commonly seen at higher concentrations (Kevin *et al*. 2014). The mercury present in soil and water is converted by micro-organisms into methyl mercury. Methyl mercury is a toxin; accumulate with fish age. US Environmental Protection Agency (EPA) has declared the mercuric chloride and methyl mercury highly carcinogenic factors. Nervous system is sensitive to all the types of mercury as its increased exposure alters the functions of brain and lead to shyness, memory problems, tremors, irritability and also leads to changes in vision or hearing (Haley 2005). For shorter time periods exposure with metallic mercury vapors at elevated levels can leads to the damage of lung, diarrhea, nausea, vomiting, skin rashes, increased blood pressure or heart rate (Tchounwou *et al*. 2008). Common symptoms of organic mercury poisoning include depression, headache, tremors, fatigue, hair loss and problems related to memory, since these symptoms are common to other conditions so it is difficult to diagnose such cases (Martin *et al*. 2009). The present standard for daily drinking water has been set by Environmental Protection Act and World Health

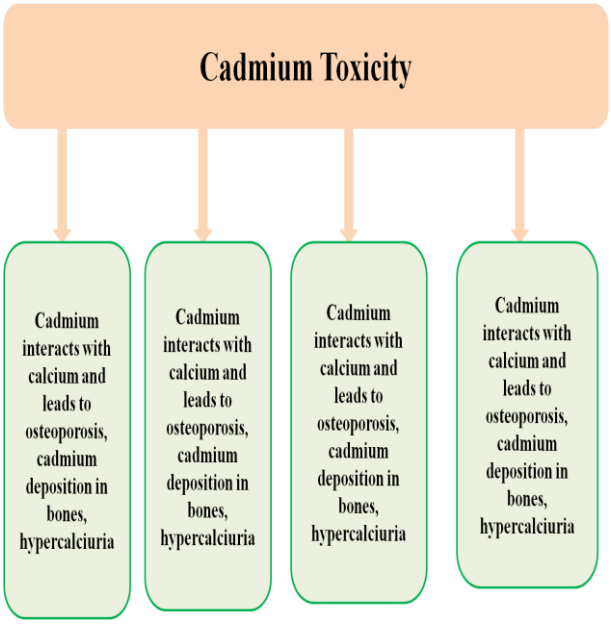
Organization at lower levels of mercury within 0.001- 0.002 mg/L due to the excess health effects related with the exposure to mercury.

2.4: Cadmium

In world ranking cadmium is seventh most toxic heavy metal as per Agency for Toxic Substances and Disease Registry (ATSDR). Cadmium is the by-product of the zinc creation, humans or animals may get exposed to this metal during the work hours or in the environmental surroundings and it will accumulate inside the human body throughout life after it was absorbed by it (Valko *et al* 2005). The cadmium was first time used in the World War I, as a replacement for tin and also in the paint industries as a pigment. Now a day it is used in the rechargeable batteries, for the special alloys production and is also present in tobacco smoke. Human beings may get primarily exposed to this toxic heavy metal via inhalation and ingestion and can cause acute to chronic intoxications (Zhang *et al*. 2004). Cadmium spread in the environment may remain in the soils and sediments for decades, plants gradually take up accumulated metals along the food chain and ultimately reach in to the human body because cadmium is predominantly found in the fruits and vegetables due to its high rate of soil to plant transfer (Bernard *et al*. 2008). Cadmium is one of highly toxic non-essential heavy metal as it is well recognized of its adverse influence on the enzymatic systems of the cells, oxidative stress and also cause nutritional deficiency in plants (Irfan *et al*. 2013).

2.4.1: Mechanism of cadmium toxicity

Toxicity mechanism of cadmium is not yet understood clearly but its effects on the cells are known as per some research reports (Suwei *et al*. 2001). The concentration of cadmium increases 3,000 fold as it binds to the cystein-rich protein (metallothionein) which forms the cystein-metallothionein complex. This cystein-metallothionein complex causes the hepatotoxicity in liver and it circulates to the kidney were it causes nephrotoxicity after its accumulation in renal tissue (Sabolic *et al*. 2010). The ability of cadmium to bind with the ligands of cystein, aspartate, histidine and glutamate can lead to deficiency of iron (Castagnetto *et al*. 2002). Cadmium is having oxidation state same as that of zinc, due to which cadmium can replace zinc which is present in metallothionein, thereby inhibiting it from acting as a free radical scavenger within the cells.



2.4.2: Effects of Cadmium on humans

20th century cadmium metal has many applications in different types of batteries, plastics, pigments, metal coatings and is used widely in electroplating (Cheng *et al*. 2014). Coal and mineral fertilizers in soils and rocks contain some amount of cadmium. Recent reports of the International Agency for Research on Cancer, cadmium and its compounds are classified by as group 1 carcinogens for humans (Chakraborty *et al*. 2013). During natural activities cadmium is released into environment by weathering, river transport, volcanic eruptions and various human activities (mining, smelting, tobacco smoking, incineration of municipal waste, and manufacture of fertilizers). Although emissions of cadmium have been evidently reduced in most of industrialized countries but still it is remains alarming source of fear for workers and people who are living in the polluted areas (Richter et al. 2017 and Chakraborty *et al*. 2013). Kidneys are the most affected organ by toxicity of cadmium as it accumulates itself in the proximal tubular cells in higher concentrations and it may also cause bone mineralization (through bone damage or by renal dysfunction). Past and present Studies of research on humans and animals have showed

that the skeletal damage is one among a critical effect of cadmium exposure along with disturbances in the calcium metabolism which results in renal stone formation and hypercalciuria. Cadmium can cause severe damage to the lungs on higher Inhaling levels and if it is ingested with higher amounts that may lead to the stomach irritation and cause vomiting and diarrhea. Long exposure time at lower concentrations cadmium deposits in the kidneys leads to the nephropathy, fragile bones and lung damage (Richter *et al*. 2017). Smokers are extra prone to cadmium intoxication than non-smokers it is because tobacco is main source of cadmium uptake in smokers (tobacco plants can accumulate cadmium from the soil) (Yadav *et al*. 2010)**,** yet cadmium uptake during other pathways is much lower but it can interact with essential nutrients and cause its toxicity effects (Donald *et al*. 1999).

2.5: Chromium

Chromium occurs in several oxidation states as Cr^{2+} to Cr^{6+} in the environment and is seventh most abundant element on the earth. The most commonly occurring forms of Cr are trivalent Cr^{+3} and hexavalent- Cr^{+6} both states being toxic to animals, humans and plants (Mohanty *et al*. 2013 and Neeshu *et al*. 2016). Chromium production naturally occurs by the burning of oil and coal, petroleum from ferrochromate refractory material, pigment oxidants, catalyst, fertilizers, chromium steel, oil well drilling and metal plating tanneries (Jacobs *et al*. 2005). Chromium is released by anthropogenically in the environment via sewage and fertilizers (Ghani *et al*. 2011). Reduced Cr (III) form of it is immobile and is insoluble in water, whereas in oxidized state Cr-(VI) it is highly soluble in water and thus is mobile (Oliveira 2012, Gurkan *et al*. 2012). Cr (III) resides in organic matter of the soil and aquatic environment in different form (oxides, hydroxides and sulphates) (Cervantes *et al*. 2001). Chromium is used mainly in industries as electroplating, metallurgy, paint and pigment formations, tanning, wood preservation, production of chemical, pulp and paper. All these industrial activities contribute to chromium pollution which is having an adverse effect on the biological and ecological species (Ghani *et al*. 2011). Toxic level of chromium in the environment due to range of industrial and agricultural practices is today's concern for the researchers, particularly hexavalent chromium, has been greatest concern (Zayed t al. 2003 and Economou *et al*. 2012). Due to discharge of the industrial wastes and ground water, the contamination of chromium has increased severely in soil. During the manufacturing of chromate, the deposit of Cr residues and waste water irrigation posed serious chromium pollution to the farmland (Bielicka *et al*. 2005). By the implementation of the modern agriculture industries and modern agricultural techniques there is continuous release of Chromium into the environment by means of the Chromium residues. Chromium dust and chromium waste water irrigation resulting in soil pollution which affects soil vegetable system and also disturbing vegetable yield and its quality for human beings (Duan *et al*. 2010). In excess presence of the chromium ahead of the permissible limit, it is critical to plant life because it severely affects the biological system of plants and enters in to food chain on consumption of these plant materials (Ghani 2011). Some enzymes as peroxidases, catalase, and cytochrome oxidases work properly in the presence of iron as their component are affected by chromium toxicity (Chandra and Kulshreshtha 2004).

2.5.1: Mechanism of chromium toxicity

Usually trivalent chromium Cr (III) is safe because of its weak membrane permeability property in the environment but instead of it hexavalent chromium Cr (VI) on the other side is more active in cell membrane penetration through passages for isoelectric and isostructural anions such as SO_{42} and HPO_4 channels and these chromates are taken up through phagocytosis. The hexavalent chromium is a strong oxidizing agent because of this property it can be reduced to produce the ephemeral species of pentavalent and tetravalent chromium, which are different from those of Cr (III). Glutathione stabilizes the pentavelent form of chromium and hence intracellular reduction of Cr [VI] is considered a detoxification mechanism when it occurs away from target region. However if intracellular reduction of Cr [VI] occurs near the target site, it may serve to activate chromium. Reactions

between Cr (VI) and biological reductants (thiols and ascorbate) results in the production of reactive oxygen species (superoxide ion, hydrogen peroxide, and hydroxyl radical) which ultimately leads to oxidative stress in the cell, ultimately damage the DNA and proteins (Zhitkovich 2005). The Cr (VI) as per the past and present research surveys has been found very much hazardous than that of Cr (III), since Cr (VI) enters into the cells more readily than does Cr (III) and is ultimately reduced to Cr (III). Because of its mutagenic properties of Cr (VI), it is categorized among group 1 human carcinogen by the International Agency for the Research on Cancer (Paul *et al*. 2012).

2.5.2: Effects of Chromium on humans

Chromium exists in nature as solid, liquid, gas and is present in rocks, soil, animals and plants (Zayed t al. 2003). Its compounds are especially much persistent in water sediments and are present in different states (divalent, four-valent, five-valent and hexa-valent state). Among these stats chromium III and VI are the most stable and their relation with human exposure is of the high interest. Compounds of chromium VI as calcium chromate, zinc chromates, strontium chromate and lead chromates are very much toxic and carcinogenic in nature while on the other hand chromium III is an essential nutritional supplement for animals and humans, it is because of its important role in glucose metabolism (Zhitkovich 2005 and Martin *et al*. 2009). Some of research reports suggest that cigarettes contained 390 g/kg of chromium, but yet there has been no significant report published any were on the amount of chromium inhaled through smoking. The exposure with chromium compounds may result in the formation of ulcers, which will persist for months and heal very slowly. These chromium causing ulcers on the nasal septum are very common in chromate workers. Exposure with the higher amounts of chromium compounds in humans can lead to inhibition of enzyme erythrocyte glutathione reductase, this inhibition lowers the capacity to reduce methemoglobin to hemoglobin (Stephen *et al*. 2013). Results of some in vitro and in vivo experimental studies have shown that the chromate compounds may induce DNA damage, which can lead to the formation of DNA adducts, chromosomal aberrations, sister chromatid exchanges, alterations in replication and transcription of DNA **(**Matsumoto *et al*. 2006 and Zhitkovich 2005).

2.6: Aluminium

Aluminium is third most abundant element found in the earth's crust and occurs naturally in the air, water and soil (Gupta*et al*. 2013). Some research studies on environmental toxicology revealed that aluminium in current scenario is a major threat for disease cause in humans, animals and plants (Barabasz *et al*. 2002). Aluminium toxicity is influenced greatly by pH of water and organic matter content, as on decreasing pH its toxicity increases. The mobilization of the toxic aluminium ions with the result of changes in pH of the soil and water by acid rains and increasing acidification of surrounding atmosphere has an adverse effect on the environment. All this effects the environment by drying of forests, crop decline or failure, plant poisoning, death of aquatic animals, and also by various imbalances in the function of human and animal systems (Barabasz *et al*. 2002). Soil surface PH, below five can lead to soil acidity that affects crop production, which it is the main concern around the world. Silicon gets leached due to acid soils and leaving behind aluminium in solid unstable form as aluminium oxyhydroxides, these unstable forms of aluminium gets discharge into phytotoxic Al^{3+} well-known as $Al(OH)^{63}$ in soil. On contact of Al^{3+} with apoplastic, plasma membrane, and symplastic targets leads to the toxicity and distracts the physical and cellular processes in the plants (Bezak *et al*. 2001). High concentrations aluminium is very toxic for aquatic animals, especially for gill breathing organisms (fish, seaweeds and crawfish) causing osmoregulatory failure by destructing the plasma and hemolymph ions (Olaniran *et al*. 2013). Metabolic pathways (phosphorous, fluorine, calcium and iron) of living organism are affected by aluminium and it was also found in some research studies that aluminium is very harmful to nervous, osseous and hemopoietic cells (Gupta*et al*. 2013).

2.6.1: Mechanism of aluminium toxicity

Most of the physical and cellular processes are affected by aluminium intervention but mechanism of absorption of aluminium by gastrointestinal tract is not understood exactly yet. As per some research surveys, it is very much difficult to give a right time period for the aluminium toxicity because some symptoms of aluminium toxicity that can be detected in seconds and others in minutes after exposure to aluminium (Monisha *et al*. 2014, Kochian *et al*. 2005)**.** In humans Mg^{2+} and Fe^{3+} are replaced by Al^{3+} on higher concentrations of aluminium and which can lead to many disturbances which are associated with intercellular communication, cellular growth and secretary functions. The different changes evoked by aluminium in neurons are similar to that of degenerative lesions observed in Alzheimer patients, the greatest complications of the aluminium toxicity are neurotoxicity effects as neuronal atrophy in the locus ceruleus, substantia nigra and striatum (Davit *et al*. 2017).

2.6.2: Effects of Aluminium on humans

Aluminium exists only in one oxidative state (3+) in the environment, its main route of consumption by humans are through inhalation, ingestion, dermal contact. Its sources of exposure are drinking water, beverages, food, and aluminium containing drugs (Yokel *et al*. 2007). Humans absorb aluminium and its compounds poorly, although it is not clearly studied yet. The symptoms of higher amounts of aluminium in humans are Nausea, vomiting, mouth ulcers, skin rashes, skin ulcers, diarrhea and arthritic pain but these symptoms are however reported to be mild and short lived (Clayton 1989). The exposure of aluminium in humans is probably a risk factor for the onset of Alzheimer disease as hypothesized by the world health organization and showed adverse effects on the nervous system and resulted in loss of memory, problems with balance and loss of coordination (Valko *et al*. 2005)**.** It is difficult in kidney patients to eliminate the aluminium from the body accumulation of aluminium in the body and leads to bone and brain damage. Higher levels of aluminium exposure can change the evolution of secondary hyperparathyroidism, leading to other diseases such as aluminium-induced a dynamic bone disease and aluminium-induced osteomalacia, both of which are characterized by low-bone remodeling. Dusty environmental life style, long-term intravenous nutrition, diminished kidney function, hemodialysis are some factors that would be the reason for the development of aluminium toxicity. Patients who are going to kidney dialysis may get exposed to aluminium present in contaminated dialysates and phosphate binders.

2.7: Iron

Iron is second most abundant metal on the earth's crust; it occupies 26^{th} elemental position in the periodic table and is a most crucial element for growth and survival of almost all living organisms (Mohanty *et al*. 2013). Iron is one of the very important components of some organisms (algae), some enzymes (cytochromes and catalase) and oxygen transporting proteins (hemoglobin and myoglobin). Due to the inter-conversion between ferrous (Fe^{2+}) and ferric (Fe^{3+}) ions iron is main transition metal for various biological redox processes **(**Valko *et al*. 2005)**.** Source of iron in the surface water is anthropogenic and is related to mining activities **(**Manoj *et al*. 2012). The simplified oxidation reactions for ferrous and ferric iron are as below.

$2FeS_2 + 7O_2 \rightarrow 2FeSO4 + H_2SO_4$ (ferrous)

$4FeSO_4 + O_2 + 10H_2O \rightarrow 4Fe(OH)_3 + 4H_2SO_4$ (ferric)

Concentration of dissolved iron in Deep Ocean is normally 33.5 × 10–9 mg/ L or 0.6 nM. Its concentration it is low in freshwater with a detection level of 5 µg/L – ICP, whereas in groundwater the dissolved iron concentration is very high with the level of 20 mg/L **(**Monisha *et al*. 2014) In some countries most of people have been exposed to high levels of iron via drinking water when collected groundwater exceeded the permissible limit on the quality of drinking water (Addisu and Asmelash 2016). Precipitation of iron will cause significant damage by means of the clogging action and it also hinders the respiration of fishes which directly affects the fishers industry (Michael *et al*. 2017). The growth

of aquatic seed species on iron toxicity was found to be inhibited by the concentration of 1 mg/L total iron as high uptake of Fe^{2+} by roots, acropetal translocation into leaves, bronzing of rice leaves and yield loss (Manoj *et al*. 2012).

2.7.1: Mechanism of iron toxicity

On failing of absorbed iron binding with the proteins various harmful free radicals are formed due to these free radicals concentration of iron is severely affected in mammalian cells (especially gastrointestinal tract) and biological fluids. After entering of extreme levels of iron into body crosses the rate limiting absorption step becomes saturated and this free iron penetrates into the cells of liver, heart and brain. Ferrous iron is converted into the ferric iron after the disruption of oxidative phosphorylation by this free iron, this ferric iron releases the hydrogen ions which increase the metabolic acidity. Free iron can also leads to the lipid peroxidation, which results in the severe damage to microsomes, mitochondria and other organelles of the cell (Albretsen 2006). Various types of free radical formation occurs due to excess intake of iron which are believed to be cause potential cellular damage e.g free radicals produced by excess iron results in cellular damage, mutations in DNA and malignant transformation which intern causes different diseases **(**Grazuleviciene *et al*. 2009).

2.7.2: Effects of Iron on humans

Most of the reactions mediated by iron support the aerobic organisms during the process respiration. If iron is not shielded properly, it can catalyze the reactions which are involved in the formation of radical intern these radicals can damage biomolecules, cells, tissues and the whole organism. In pediatricians iron poising has always been topic of interest because children are highly susceptible to the iron toxicity as they are maximum exposed to iron containing products (Chaim 2007). Iron toxicosis occurs via four stages (i): iron toxicosis after 6 hrs of iron overdose is marked by gastrointestinal effects (gastro intestinal bleeding, vomiting and diarrhea). (ii): iron toxicosis within 6-24 hrs of iron dose is considered as period of apparent medical recovery (latent period). (iii): iron toxicosis between 12-96 hrs of iron dose is marked by shocks, lethargy, tachycardia, hypotension, hepatic necrosis, metabolic acidosis and sometimes death. (iv): iron toxicosis within 2-6 weeks of iron dose is marked by the formation of gastrointestinal ulcerations and development of strictures (Matthew 1979 and Hillman 2001).

There is a serious problem of excess iron uptake in developed and meat eating countries because it increases the risk of cancer. The workers who are highly exposed to the asbestos almost contains thirty percent of iron are at high risk of asbestosis, this asbestosis is considered second most important cause for the lung cancer. Free radicals may be the important cause for lung cancer because asbestos associated cancer is linked to free radicals (Ghosh *et al*. 2007). Free radicals are actually neutralized by different enzymes (superoxide dismutase, catalase and glutathione peroxidases). The superoxide molecule has the ability to release iron from ferritin and that free iron reacts with more and more of superoxide and hydrogen peroxide forming highly toxic free radicals such as hydroxyl radical. Hydroxyl radicals are dangerous as they can inactivate certain enzymes, initiate lipid peroxidation, depolymerize polysaccharides and can cause DNA strand breaks which can sometimes result in cell death (Kochian *et al*. 2005, Fine 2000 and Hershko *et al*. 1998,). The salts of iron as iron sulfate, iron sulfate monohydrate and iron sulfate heptahydrate are of low acute toxicity when exposure is through oral, dermal and inhalation routes and hence they have been placed in toxicity category three, furthermore iron salts are considered to be safe by the food and drug administration as their toxic effects are very much negligible (Fine 2000).

3: Preventable measures for heavy metal poisoning

The most important step is determination of source and removal of it, so that exposure can be stopped. These include recognition of exposures in the home, work places and the surrounding environment.

Some simple ways to prevent exposure to heavy metals includes:

✓ Before going inside your home remove your shoes and limit the dust, since metals may be present in dust and dirt.

✓ Aware local fish advisories for mercury or arsenic.

✓ Aware your whole family regarding lead sources that may be in the home such as peeling paint, imported toys, or imported candies.

✓ If your job involves working with metals, make sure you do not bring any metal residue or powder home. This may include showering and changing clothes at work before coming home.

✓ Be aware of any industrial sources (operating or closed) that may be close to your home or neighborhood.

✓ If you have hobbies that involve working with metals, make sure the area is well ventilated. Wash your hands when you are finished.

✓ If you have older plumbing in your home, consider having your drinking water tested for metals.

✓ If you are using a well for your drinking water, you may want it tested for inorganics (includes metals)

Conclusion

In this review we summarized the effects of arsenic, lead, mercury, cadmium, chromium, aluminum and iron on living organisms and surrounding environment. Failure in heavy metal exposure can cause severe complications in future because of their adverse effects on living organisms and surrounding environment. Monitoring the exposure and probable intervention for reducing additional exposure to heavy metals in the environment can become a momentous step towards prevention. National as well as international co-operation is vital for framing appropriate tactics to prevent heavy metal toxicity and major occupational exposure to the heavy metals can be decreased by improving the engineering solutions. Large population screening based studies are to be needed to discover the strategies to control the adverse effects of metal toxicity besides effective legislation, guidelines and detection techniques need to be put in place to control the heavy metal toxicity to living organisms and their surrounding environment.

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